

Prospective Nationwide Study of *Aeromonas* Infections in France[▽]

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We report a systematic prospective multicenter nationwide study of clinical *Aeromonas* infections in France. During 6 months (May to October 2006), 78 cases of aeromonosis were reviewed for risk factors and clinical, microbiological, and antimicrobial susceptibility data. They included wound infections (44%), bacteremia (26%), enteritis (19%), respiratory tract infections (6%), and miscellaneous (5%) infections.

Aeromonas species are opportunistic pathogens involved in various types of infections. Previously published epidemiological studies are usually limited to one type of infection, and global epidemiological studies are scarce. In Europe, the studies were rare, retrospective, and restricted to a few cases and/or they involved lengthy study periods with epidemiological changes during their course (3, 24, 29, 34). To complete these epidemiological data, we present an overview of the characteristics of all types of *Aeromonas* infections occurring in France during a short defined period including warm months based on a prospective multicenter nationwide study (70 hospitals).

During 6 months (May to October 2006), all patients from whom an aeromonad was isolated were included. Cases were categorized as definite, possible, and doubtful infections, based on data prospectively collected from standardized records. Definite and possible infections included isolation of an *Aeromonas* bacterium either from a sterile site or in pure culture (definite infection) or in mixed culture (possible infection), clinical and biological signs of infection, exclusion of other etiologies, and decision to treat. Doubtful infection included isolation of an *Aeromonas* bacterium, no clinical signs of infection, and decision not to treat. Cutaneous and pulmonary exposure to a potential *Aeromonas*-contaminated environment (water and soil) was recorded from the medical history. Community-acquired infection was defined by *Aeromonas* culture from a first specimen obtained less than 48 h after admission. Strains were identified with partial sequence analysis of the *rpoB* gene, including sequences of all 19 known *Aeromonas* species type strains, as reported elsewhere (20, 22). Antimicrobial susceptibility was tested with the disk diffusion method on Mueller-Hinton agar according to the guidelines of the Comité de l'antibiogramme de la Société Française de Microbiologie (6). Qualitative variables were compared with the chi-square test or Fisher's exact test where appropriate.

Out of the 99 included patients, 78 (79%), were considered

infected. The infection was nosocomial in six cases (7%). Seventy of the 84 *Aeromonas* isolates recovered from these 78 patients were studied. The disease distribution, patient characteristics, and risk factors are shown in Table 1. Differences in age, sex ratio, comorbidity, and environmental exposure frequencies were noted across types of infection. Interestingly, wound and skin soft-tissue infections (SSTI), followed by bacteremia, were the most prevalent infections, as reported elsewhere (9).

Wound infections and SSTI (34 cases) consisted of purulent wound infection (25 cases, 74%) and soft-tissue abscesses (nine cases, 26%). These infections mainly occurred in otherwise healthy patients (88%), among whom young men predominated. Rates of trauma and of environmental exposure concomitant with the trauma (both >90%) were among the highest reported (10, 13, 16, 31). Injuries with water exposure (15 cases) involved only freshwater, as reported elsewhere (31), and resulted mainly from leisure activities (14 cases). Injuries with soil exposure (15 cases) involved penetrating wounds (five cases) or road accidents (10 cases). These characteristics are in keeping with the literature (9, 13, 16). No cases were related to leech therapy. This occasional etiology, related to reconstructive surgery, could be underrepresented in our series because this type of surgery is underpracticed in our participating hospitals (9, 30). Finally, wound infections and SSTI required surgical or antimicrobial treatment in 23 (68%) and 29 (85%) of the 34 cases, respectively. Interestingly, initial antibiotic treatment was inappropriate for 18 of the 29 patients (62%).

Patients with bacteremia (20 cases) showed characteristics that differed somewhat from published data (7, 14, 18, 23, 29). Females were as numerous as males. Six (30%) patients had no underlying health disorders, a rate higher than that reported elsewhere (7, 12, 14, 17, 23). Among these, very elderly patients predominated (five patients of >80 years and four patients of >90 years). These noteworthy features suggest, like the results from the work of Llopis et al. (24), that *Aeromonas* bacteremia is associated with very elderly and otherwise healthy patients and may become more frequent as Western populations age. The distribution of comorbidities associated with *Aeromonas* bacteremia (Table 1) was similar to that reported in the United States and Europe (14, 24, 29) but dif-

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TABLE 1. Clinical characteristics, risk factors, and microbiological characteristics for *Aeromonas* infections in France

Characteristic	Value for infection type:						<i>P</i> value ^a
	All	Wound infection and SSTI	Bacteremia	Gastroenteritis	RTI	Other	
No. of patients (%)	78 (100)	34 (44)	20 (26)	15 (19)	5 (6)	4 (5)	
Age, mean (yr)	52	43	72	50	48	NE ^e	
Sex ratio	1.7	1.6	1.2	2	5	NE	
No. of definite infections/no. of possible infections		14/20	14/6	0/15	1/4	1/3	
White blood count, median (g/liter) (25th percentile; 75th percentile)	11.6 (9; 14.3)	12.7 (10; 14.6)	11.4 (7.4; 15.6)	9.2 (6; 12.4)	11.6 (8.4; 14)	NE	
C-reactive protein level, median (mg/liter) (25th percentile; 75th percentile)	38 (16; 139)	58 (31; 141)	99 (44; 144)	37 (3; 64)	258 (10; 290)	NE	
No. of cases with environmental exposure (%)	35 (44.8)	31/34 ^b	1/20	ND ^f	3/5	0	<0.001
Freshwater	19 (24.3)	15	1		3		
Soil	15 (19.2)	15					
No. of cases with wound concomitant with environmental exposure (%)	34 (43.6)	33	1				<0.001
No. of cases with comorbidity (%)							
None	48 (61.5)	30	6	6	2	4	<0.001
Malignancy	15 (19.2)		8	6	1		<0.001
Immunosuppression	11 (14.1)		7	3	1		<0.001
Diabetes mellitus	6 (7.7)	2	2	2			0.77
Alcoholism	5 (6.4)	1	3		1		0.33
Other ^c	4 (5.1)	1	1	1	1		
≥2 comorbidities	11 (15.1)	0	7	3	1		0.001
Species distribution							
Total no. of strains (%)	70 (100)	34 (100)	16 (100)	12 (100)	5	3	
<i>A. hydrophila</i>	25 (35.7)	19 (55.8)	1 (6.3)	2 (16.7)	2	1	0.001^d
<i>A. caviae</i>	15 (21.4)	3 (8.8)	7 (43.8)	5 (41.7)			0.006^d
<i>A. veronii</i>	28 (40.0)	12 (35.3)	7 (43.8)	5 (41.7)	3	1	0.73
<i>A. allosaccharophila</i>	1 (1.4)		1 (6.3)				
<i>A. jandaei</i>	1 (1.4)					1	
No. of cases with polymicrobial growth (%)	33/78 (42.3)	20/34 (58.8)	6/20 (30.0)		4/5 (80.0)	3	

^a Entries for which the *P* values were significant (≤ 0.05) are in boldface (analysis including all groups except "other" infections).

^b Data unavailable in three cases.

^c Chronic renal failure ($n = 1$), Crohn's disease ($n = 1$), trisomy 21 ($n = 1$), and chronic respiratory failure ($n = 1$).

^d Further statistical analysis showed that *A. hydrophila* was more frequent in wound infections than in other infections ($P = 0.0008$) and less frequent in bacteremia than in other infections ($P = 0.006$) and that *A. caviae* was more frequent in bacteremia than in other infections ($P = 0.03$) and less frequent in wound infections than in other infections ($P = 0.0077$).

^e NE, not evaluable.

^f ND, food consumption not determined.

ferent from that reported in Asia (7, 18, 23, 37). In Asia, the higher prevalence of liver and biliary diseases combined with the higher frequency of *Aeromonas* intestinal carriage could explain the observed difference from Western countries (4, 7, 36). Gut was the suspected source in all of our patients. Biliary tract disease was frequent (7 cases of 20, 35%). This disease should therefore be sought in cases of *Aeromonas* bacteremia. In contrast to previous reports, *Aeromonas* bacteremia was never related to wound and SSTI in our series (18, 23, 24). The overall fatality rate was 35% (7 patients of 20). Interestingly, this rate was 17% (one of six) in the group of elderly patients with no comorbidity and 43% (6 of 14) in the group of younger patients with comorbidities.

Aeromonas species as a causative agent of gastroenteritis remain controversial due to digestive carriage and weak evidence of enteropathogenicity (13, 36). Still, our series comprised 15 cases of gastroenteritis, suggesting that *Aeromonas*-

associated diarrhea is rare in France or does not require hospital management. Malignancy was present in six (40%) cases (Table 1). This high rate could be related to the population studied, namely, hospitalized patients. However, higher digestive tract colonization by *Aeromonas* and a subsequently higher risk of diarrhea have been suggested in neutropenic patients with hematologic malignancies, although our series dealt instead with solid malignancies (32).

Our series included five cases of respiratory tract infection (RTI), with clinical severity, a preponderance of males, comorbidity, and/or massive aquatic environmental exposure. Three of our patients were near-drowning victims, a frequent risk factor (2). The involvement of *Aeromonas* species recovered from sputum remains difficult to establish, particularly when other pathogens are found. However, several cases of severe infection have been reported with *Aeromonas* species in mixed culture (2). Given that *Aeromonas* is now recognized as a

TABLE 2. Susceptibilities of *Aeromonas* isolates recovered from infected patients^a

Antimicrobial agent	Type of susceptibility within all isolates (%) (n = 70)			Susceptibility within species (%)			
	S	I	R	<i>A. caviae</i> (n = 15)	<i>A. hydrophila</i> (n = 25)	<i>A. veronii</i> (n = 28)	P value
Amoxicillin	2.8	2.8	94.4	6.7	0.0	3.7	0.693
Co-amoxiclav	18.1	81.9		40.0	15.4	11.1	0.078
Ticarcillin	9.7	19.4	70.8	20.0	11.5	3.7	0.169
Ticarcillin + clavulanate	76.4	8.3	15.3	86.7	80.0	66.7	0.35
Piperacillin	95.8	1.4	2.8	100.0	88.4	100.0	0.054
Piperacillin + tazobactam	95.8	1.4	2.8	100.0	88.4	100.0	0.054
Cephalothin	47.2	9.7	43.1	20.0	11.5	100.0	<0.001
Cefotaxime	95.8	4.2		100.0	92.3	100.0	0.178
Ceftazidime	98.6		1.4	100.0	100.0	100.0	1
Cefepime	98.6		1.4	100.0	100.0	96.3	1
Imipenem	68.1	31.9		93.3	84.6	37.0	<0.001
Ciprofloxacin	91.7	2.8	5.6	93.3	84.6	100.0	0.07
Gentamicin	100.0			100.0	100.0	100.0	1
Tobramycin	65.3	16.7	18.1	93.3	84.6	29.6	<0.001
Amikacin	98.6	1.4		100.0	100.0	96.3	1
Tetracycline	88.9		11.1	100.0	84.6	88.9	0.35
Co-trimoxazole	87.5	4.2	8.3	80.0	80.8	100.0	0.017

^a Entries for which the *P* values were significant are in boldface (Fisher's exact test, significance set at 0.05). S, susceptible; I, intermediate; R, resistant.

respiratory tract pathogen, although rarely encountered (2, 11, 13, 15, 25, 26, 28, 33), our cases with mixed culture were categorized as "possible infection" to better reflect the RTI frequency.

Finally, four specific infections included ocular infection, hepatobiliary infection, urinary tract infection, and peritonitis with mesenteric ulcer perforation, all occasionally reported (4, 5, 13, 27).

Sixty-nine (99%) of the 70 *Aeromonas* isolates analyzed belonged to "clinically relevant" *Aeromonas* species (Table 1) (8, 13). The species isolated here were similar to those reported elsewhere (13), although their distribution differed somewhat (1, 19), probably due to the identification method used, use of an updated taxonomy, and the geographical location of the study. *Aeromonas hydrophila* was less frequent in bacteremia (*P* = 0.006) and more frequent in wound infections (*P* = 0.0008) than in other infections. *Aeromonas caviae* was less prevalent in wound infections (*P* = 0.0077) and more prevalent in bacteremia (*P* = 0.03) than in other infections. *Aeromonas veronii* was not associated with a particular type of infection. Culture yielded polymicrobial growth in 33 (42%) infected patients (from 30% for bacteremia to 80% for RTI [Table 1]), data in keeping with previous reports (7, 16–18, 23, 24, 29, 31, 35). In seven samples (9% of samples), more than one strain of *Aeromonas* was isolated, mainly from patients with wound infections or SSTI, suggesting an exposure to an environment with high *Aeromonas* diversity (21). Such cases might be underestimated, as microbiologists may not systematically search for mixed aeromonad cultures.

The analysis of antimicrobial susceptibility (Table 2) showed a low rate of co-amoxiclav susceptibility, which is of concern because wound infections are often empirically treated with this drug (in this study, 14 of the 29 wound cases [47%] treated with antibiotics). Given the high rate of mixed infections, the lack of specific clinical signs of *Aeromonas* infection, the current susceptibility data, and the previous reports, the most active empirical treatments would consist of a broad-spectrum

cephalosporin or a fluoroquinolone, combined with gentamicin or amikacin in cases of severe infection (18).

In summary, we report a detailed overview of *Aeromonas* infections encountered in a temperate European country during the warm months, with an update on antimicrobial susceptibility that should be useful for patient management.

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